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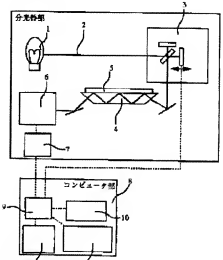
(54) **BLOOD ANALYZER**

(57) Abstract:

PURPOSE: To realize biochemical inspection of blood immune to disturbance components at low cost.

CONSTITUTION: An infrared light 2 from an infrared light source 1 passes through an interferometer 3 and enters into a damping total reflection prism 4 where the infrared 2 repeats total reflection and a specific wavelength thereof is absorbed by a sample 5 introduced onto the prism 4 before the infrared light 2 enters into s detector 6. A detection signal is delivered from the detector 6 to a computer section 8 through an AD converter 7. The computer section 8 comprises a CPU 9, an output unit 10, an input unit 11, and a memory 12 and the detection signal is processed numerically before being converted into a spectrum. The absorbance in the wave number region of characteristic absorption band is sampled from the spectrum of the sample for the objective component to be measured and the concentration thereof is calculated according to a working formula stored in the memory 12. The concentration is calculated using a standard liquid group containing disturbance components of abnormal concentration according to the working formula free from the influence of disturbance components. This constitution realizes an easy maintenance calibration free analyzer.



DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Industrial Application]This invention relates to the analysis apparatus which measures a blood biochemistry ingredient.
[0002]
[Description of the Prior Art]It is related with the blood biochemistry analysis using infrared spectroscopy, and is applied. The 95th page is described from spectroscopy (Applied spectroscopy) (1994), the 48th volume, and the 85th page. In this art, by infrared spectroscopy, measure the concentration of seven ingredients of glucose in human plasma, the quality of total protein, total cholesterol, triglyceride, urea, and uric acid, and as a reference solution, Use the human plasma which collected blood from the patient, and the density range of the ingredient in a reference solution mentioned above, respectively, They are 36 - 482 mg/dl (deciliter), 59-83 g/l (liter), 125 - 329 mg/dl (deciliter), 47 - 640 mg/dl (deciliter), 14 - 69 mg/dl (deciliter), and 2.1 - 9.8 mg/dl (deciliter).
[0003]About the measuring method of the blood automatic analyser using the enzymatic process used for the clinical laboratory test from the former, the 49th page is described from the 44th page in the volume "automatic analysis for clinical", and for Kyoichi Ozawa, and (1985). The proofreading which used the reference solution is described by this method.
[0004]
[Problem(s) to be Solved by the Invention]In the blood biochemistry analysis using the conventional infrared spectroscopy, it was not taken into consideration about the interaction between ingredients, but when it became more than the density range of the reference solution group which a certain constituent concentration in a sample uses for proofreading, there was a problem of the ingredient having turned into an interfering component in the density measurement of other ingredients, and becoming a cause with error. In order to use a lot of reference solutions for proofreading, there was a problem that time and cost started proofreading.

[0005]In the hemanalysis meter using the conventional enzymatic process, the proofreading which used the reference solution of one day was required, quality control was complicated, and in order to use reaction reagents, such as an enzyme, for measurement, the running cost was high by futility, such as a dead stock of a reagent.
[0006]The purpose of this invention is to be able to measure and to provide the hemanalysis meter which does not need a reagent, a reference solution, etc., without solving the above-mentioned problem and being influenced by an interfering component.
[0007]
[Means for Solving the Problem]In order to solve the above-mentioned problem, a reference solution group which covered a high concentration range which an interfering component in a sample can take is constituted, and an analyzer (for example, infrared spectrometer) is equipped with memory storage which memorized a measuring formula computed from a spectrum (for example, infrared absorption spectrum) of a reference solution group, and measuring object component concentration.
[0008]When it explains to details more, the feature of this invention is on following each point. (1) A means for entering in a sample light emitted from an infrared light source and a light source, It is a hemanalysis meter which has an arithmetic processing means which processes a signal by photodetector which detects light which penetrated or reflected a sample, and this photodetector, Provide a memory measure which memorizes a measuring formula for which it asked using a reference solution group containing a biochemistry ingredient of concentration which separated from a constituent concentration range in a healthy person's blood, and A measuring formula, Measuring object component concentration in blood is obtained from an infrared absorption spectrum of blood, (2) A measuring formula for which it asked using a reference solution group containing a biochemistry ingredient of concentration which separated from a constituent concentration range in a healthy person's blood, A memory measure which memorizes amendment data for amending a value computed from a measuring formula, Measuring object component concentration in blood is obtained from a measuring formula and an infrared absorption spectrum of blood, and an error of measured value of the aforementioned measuring object component is amended based on amendment data, (3) It has a memory measure which memorizes measuring object component concentration of an infrared absorption spectrum of a reference solution group, and a reference solution group containing a biochemistry ingredient of concentration which separated from a constituent concentration range in a healthy person's blood, Obtaining measuring object component concentration in blood from an infrared absorption spectrum, a measuring formula computed from constituent concentration, and an infrared absorption spectrum of blood has the feature.
[0009]A relation of an infrared absorption spectrum of two or more reference solutions and constituent concentration whose measuring object component concentration of the above-mentioned measuring formula is known, Multiple regression analysis, a principal-component-analysis method, or the second [a minimum of] power (Partial Least Squares,

PLS) of a portion analyzes with multivariable corporate evaluation system, such as law, and a multiple regression expression expresses, The above-mentioned reference solution adds an interfering component to either either human serum whose measuring object component concentration is known, human plasma or the Homo sapiens blood and these. In glucose concentration in a reference solution, 40 or more mg/dl and nature concentration of total protein Not less than 7 g/dl, It is preferred that in 3 or more mg/dl and bilirubin concentration 0.3 or more mg/dl and a cholesterol concentration range consider it as 133 or more mg/dl, and a triglyceride density range considers [creatinine concentration / 0.8 or more mg/dl and urea concentration / 7 or more mg/dl and uric acid concentration] it as 40 or more mg/dl.

[0010]Measured value by a measuring formula which obtained the above-mentioned amendment data using a sample for amendment whose at least one or more measuring object component concentration is known, It is a difference of measured value and known concentration which are produced from an error during a day of measurement, and an error between apparatus, and it is preferred to subtract and add the aforementioned difference to measured value about a blood sample, and to perform amendment about measured value.

[0011]A means to enter light in the above-mentioned sample is a sample cell, has a mechanism which introduces and discharges a sample on the surface of attenuated-total-reflection prism, and considers it as composition which spreads [which spreads and enters it] and emits light from an infrared light source to attenuated-total-reflection prism. Attenuated-total-reflection prism consists of zinc selenide, germanium, silicon, sapphire, etc., and a spectral means in a hemanalysis meter is either of the Fourier spectra which used a concave grating, a spectral prism, or an interferometer. As a memory measure, a storage of an IC memory [or] built in an arithmetic processing means, an optical disc attached to an arithmetic processing means, a magnetic disk, or a magneto-optical disc etc. is used. Any, such as an arithmetic circuit created by having a general-purpose computer generally used and a general calculation circuit means, and the exclusive purpose to a device of this invention, may be sufficient as an arithmetic processing means in this invention.

[0012]

[Function]By extending the range of the interfering component concentration in a reference solution group, the measuring formula which reduced the influence of an interfering component on the measurement of an ingredient made into a measuring object can be obtained, and highly-precise-izing of measurement and high accuracy-ization can be attained. By equipping an analyzer (for example, infrared spectrometer) with the memory storage which memorized the measuring formula computed from these reference solution groups, proofreading becomes unnecessary and a running cost becomes cheap.

[0013]

[Example]

(The first example) Based on an example, this invention is explained in detail below.

Drawing 1 expresses the hardware constitutions of the hemanalysis meter using the attenuated total reflection spectroscopy which is the first example of this invention. In the hemanalysis meter of this example, a non-reagent can perform measurement, the quality of total protein in a blood serum, urea, glucose, triglyceride, and total cholesterol, of five ingredients. After the infrared light 2 emitted from the infrared light source 1 produces phase contrast through the interferometer 3, it enters into the attenuated-total-reflection prism 4, and a specified wavelength is absorbed by the sample 5 introduced on the prism 4, carrying out total internal reflection of the inside of the prism 4, and it is emitted to the detector 6. The signal detected in the detector 6 is inputted into the computer department 8 through A/D converter 7. The computer department 8 consists of the input device 11 and the memory storage 12 which consist of the output unit 10, keyboard and mouse which consist of CPU9, a display, and a printer, and a bar code reader, The signal inputted into CPU9 is changed into a spectrum through numerical processing of the Fourier transform, phase correction, etc. The concentration of a measuring object component is computed by only the absorbance of the wave number field of the characteristic absorption band of a measuring object component being sampled, and the measuring formula memorized by the memory storage 12 of the computer department 8 being used for the sample spectrum furthermore changed into the absorbance from transmissivity. The computed concentration is displayed with the output units 10, such as a display of the computer department 8, and a printer, and the operating personnel can know an analysis result. Information, including the name about a patient, sex, etc., is inputted into a computer by the input device 11.

[0014]Drawing 2 expresses the calculation procedure of the measuring formula used in this example. In this example, the measuring formula which reduced the influence of the other ingredients on glucose was used by making an interfering component into glucose. So that a reference solution may make human serum 13 **-SU and the density range of glucose may be 2 g/dl (deciliter) from 40 mg/dl (deciliter) in this example, In accordance with [normal-values blood serum 15] the thing 14 which added the additive agent for glucose into the blood serum suitably, 100 samples were used as the semi- liquid group 16 for searching for an analytical curve. Even when ingredients other than glucose are interfering components, the measuring formula which reduced the influence of an interfering component by considering it as a reference solution preferentially etc. can be computed by the ability to add an interfering component like the case of a guru coast, or choose an abnormal value sample. For example, when the quality of total protein is an interfering component, when creatinine is an interfering component more than 7 g/dl (deciliter), the quality of total protein. When urea of more than 0.8 mg/dl (deciliter) is an interfering component, creatinine, When uric acid of more than 7 mg/dl (deciliter) is an interfering component, urea, When the bilirubin of more than 3 mg/dl (deciliter) is an interfering component, uric acid, When cholesterol of more than 0.3 mg/dl (deciliter) is an interfering component, bilirubin, Cholesterol can reduce the influence of each interfering component using the reference solution in which triglyceride has the concentration more than 40 mg/dl

(deciliter), when triglyceride of more than 133 mg/dl (deciliter) is an interfering component. With the enzymatic process which uses an automatic analyser etc., the 100 above-mentioned samples perform measurement 17 of the measuring object component concentration in a sample, and perform measurement 18 of an infrared absorption spectrum by the spectroscope part built in the hemanalysis meter of this example by one side. Make measuring object component concentration of 100 samples into the purpose variable 19, and the absorbance group of the wave number field of the characteristic absorption band of the measuring object component of the infrared absorption spectrum of 100 samples is made into the explaining variable 20, Analysis 21 by the partial minimum root squaring methods and the PLS (Partial Least Squaeres) method is conducted, and the multiple regression expression of the form of y=ax+b expresses the relation of two variables. This multiple regression expression is made into the measuring formula 22, and the memory storage of the computer department of a hemanalysis device is made to memorize.

[0015]Drawing 3 is an example of the sample cell used by this example. This sample cell is a flow cell.

The sample 5 is introduced on the attenuated-total-reflection prism 4 with the cover-printing pump 23.

In the prism 4 top, the space into which a sample goes with the covering 27 provided with O ring 24, the feed port 25 of a sample, and the outlet 26 is sealed. If the sample 5 is introduced on the prism 4 and an infrared absorption spectrum is measured, the measured sample 5 will be discharged by the waste fluid bottle 28 with the cover-printing pump 23. Furthermore, the penetrant remover included in the penetrant remover bottle 30 is introduced on the prism 4 by the change of the electromagnetic valve 29, a channel and the surface of the prism 4 are washed, and it is discharged by the waste fluid bottle 28 after the end of washing by it.

[0016]Drawing 4 is a graph showing the effect by this example. The selectivity of measurement of triglyceride to glucose which is an interfering component, cholesterol, and urea is investigated. The graph shown in drawing 4 adds glucose which is an interfering component into a certain blood serum, and expresses the measurement result (vertical axis) of the hemanalysis (based on ATR/FT-IR method) meter of total cholesterol when changing only the glucose concentration (horizontal axis) in a blood serum, triglyceride, and urea with it. - When blood serum 100 sample which does not add glucose is made into a reference solution group (conventional method), O is a case (this example) where blood serum 100 sample which added glucose is made into a reference solution group. According to the graph of this drawing 4, this example shows that measurement of each ingredient is made, without being influenced by glucose. Especially in any [of triglyceride, cholesterol, and urea] case. In a conventional method (that is, unlike this example, addition of glucose has not been carried out with the standard solution used at the time of creation of an analytical curve.), the tendency from which it separates greatly from the reference

concentration value given beforehand is seen so that the glucose concentration added as an interfering component becomes large, but. In the method by this example, it is not based on the concentration of the added glucose concentration, but the measurement result is in agreement with a reference value.

[0017]Drawing 5 is the result of measuring the quality of total protein in a blood serum, urea, glucose, triglyceride, and total cholesterol with the hemanalysis meter of this example, and the conventional enzymatic process. The value which measured the horizontal axis in drawing 5 with Hitachi 7150 automatic analyser about the quality of total protein, glucose, urea, and triglyceride, and measured it with the conventional method about Hitachi 736 automatic analyser and total cholesterol is shown, and a vertical axis is a measurement result in the ATR/FT-IR method by this example. A correlation coefficient with a conventional method is 0.98 or more, and each ingredient can measure on a par with a conventional method by the ATR/FT-IR method by this example.

[0018](The second example) Drawing 6 is a procedure of the amendment in the hemanalysis meter of the second example of this invention. The hardware constitutions of a hemanalysis meter and the calculating method of a measuring formula are the same as that of the first example. This example showed the amendment procedure of glucose. By use of the hemanalysis meter over a long period of time, this amendment is used for amendment of the error between apparatus when using a measuring formula for another hemanalysis meter, when the error during a day arises by change of the surface state of attenuated-total-reflection prism, etc. First, glucose concentration asks for the glucose concentration of the two control sera 32 and 33 which are known on the same day as the day which measured the reference solution by the analytical curve remembered to be hemanalysis 31 [a total of] by 31. The analytical curve used here proofreads by measuring a reference solution in the spectroscope part of the analyzer 31. The glucose concentration value calculated here is set to y, glucose concentration (reference value) found beforehand is set to x, the correlation straight line which revolved by a minimum of 2 multiplication and for which it asked is made into the ideal line 34, and it records on the memory storage 35. a and b in drawing 6 are inclination and the section of the ideal line 34 here, respectively. It is considered that this ideal line 34 is what was measured in the state where there is no error of hardware (hemanalysis meter) origin. Measured value is amended, when using the measuring formula memorized by hemanalysis 31 [a total of] with the same model device other than the device (hemanalysis 31 [a total of]) which measured the reference solution (when the error between apparatus arises), and when the error during a day arises in the measured value although it is the same device (hemanalysis meter). When hemanalysis 36 [a total of] which the error between these apparatus and the error during a day produced is used and a sample is measured, With the measuring formula (the same thing as hemanalysis a total of 31 measuring formulas) memorized before the start of actual sample measurement of a day by 35 which is hemanalysis 36 [a total of] and the memory storage of 36. Let the correlation straight line obtained by revolving like the time of measuring the

control sera 32 and 33, asking for glucose concentration, and asking for the ideal line 34 be the correction straight line 37 (c and d are inclination and the sections of the correction straight line 37). The correction formula 38 is computed from the data showing the ideal line 34 memorized by the correction straight line 37, and hemanalysis a total of 36 memory storage 35, and it memorizes to the memory storage 35. The value 40 (y^) which measured the blood serum 39 which is a sample by hemanalysis 36 [a total of] is included in the correction formula 38, and the correction value 41 (y) is calculated. In the above explanation, the memory storage 35 is formed in the hemanalysis of a total of 31 and 36 each.
The data memorized by memory storage can be made common using a floppy disk etc.

[0019]Drawing 7 is a figure showing the effect of this example. Drawing 7 expresses the error during a day when the sample of the same concentration is measured with a hemanalysis plan. The measured value according [according to / in a horizontal axis / time (Sun.)] to a hemanalysis meter in a vertical axis is shown. By the case where amendment as not boiled as ** shows, but shown in 6 is not performed, although measured value is high depending on measuring time, by the correcting method by this example shown by O, the error during a day is amended and it turns out that measured value is maintaining fixed accuracy and accuracy.
[0020]
[Effect of the Invention]According to this invention, it can measure, without being influenced by an interfering component, and since a reagent, the reference solution, etc. are unnecessary, it can inspect by low cost.

[Translation done.]

* NOTICES *

1.This document has been translated by computer. So the translation may not reflect the original precisely.
2.**** shows the word which can not be translated.
3.In the drawings, any words are not translated.

CLAIMS

[Claim(s)]
[Claim 1]A means for entering in a sample light emitted from an infrared light source and a light source.
An arithmetic processing means which processes a signal detected by photodetector which detects light which penetrated or reflected a sample, and this photodetector.
A measuring formula which possessed a memory measure which memorizes a measuring formula for which it asked using a reference solution group which is the hemanalysis meter provided with the above and contains a biochemistry ingredient of concentration which separated from a constituent concentration range in a healthy person's blood, and was memorized to this memory measure, Measuring object component concentration in blood is obtained from an infrared absorption spectrum of blood.

[Claim 2]A means for entering in a sample light emitted from an infrared light source and a light source.
An arithmetic processing means which processes a signal detected by photodetector which detects light which penetrated or reflected a sample, and this photodetector.
A measuring formula for which it asked using a reference solution group which is the hemanalysis meter provided with the above and contains a biochemistry ingredient of concentration which separated from a constituent concentration range in a healthy person's blood, Measuring object component concentration in blood is obtained from a memory measure which memorizes amendment data for amending a value computed from this measuring formula, a measuring formula memorized to this memory storage, and an infrared absorption spectrum of blood, and an error of said measuring object component measured value is amended based on said amendment data.

[Claim 3]A means for entering in a sample light emitted from an infrared light source and a light source.
A detector which detects light which penetrated or reflected a sample.

An arithmetic processing means which processes a signal detected by this photodetector. It has a memory measure which memorizes measuring object component concentration of an infrared absorption spectrum of a reference solution group, and this reference solution group which is the hemanalysis meter provided with the above and contains a biochemistry ingredient of concentration which separated from a constituent concentration range in a healthy person's blood, Measuring object component concentration in blood is obtained from an infrared absorption spectrum memorized to this memory measure, a measuring formula computed from constituent concentration, and an infrared absorption spectrum of blood.

[Claim 4]A measuring formula given in one claim of claim 1 to claims 3, Measuring object component concentration a relation of an infrared absorption spectrum of two or more reference solutions and constituent concentration which are known, A hemanalysis meter characterized by what multiple regression analysis, a principal-component-analysis method, or the second [a minimum of] power (Partial Least Squares, PLS) of a portion analyzes with multivariable corporate evaluation system, such as law, and a multiple regression expression expresses.

[Claim 5]A hemanalysis meter, wherein a reference solution given in one claim of claim 1 to claims 3 is either [whose measuring object component concentration is known] human serum, human plasma or the Homo sapiens blood.

[Claim 6]A hemanalysis meter, wherein a reference solution given in one claim of claim 1 to claims 3 adds an interfering component into either human serum, human plasma or the Homo sapiens blood.

[Claim 7]A hemanalysis meter in which a reference solution group given in one claim of claim 1 to claims 3 is characterized by glucose concentration in a reference solution being 40 or more mg/dl.

[Claim 8]A hemanalysis meter in which a reference solution group given in one claim of claim 1 to claims 3 is characterized by nature concentration of total protein in a reference solution being not less than 7 g/dl.

[Claim 9]A hemanalysis meter in which a reference solution group given in one claim of claim 1 to claims 3 is characterized by creatinine concentration in a reference solution being 0.8 or more mg/dl.

[Claim 10]A hemanalysis meter in which a reference solution group given in one claim of claim 1 to claims 3 is characterized by urea concentration in a reference solution being 7 or more mg/dl.

[Claim 11]A hemanalysis meter in which a reference solution group given in one claim of claim 1 to claims 3 is characterized by uric acid concentration in a reference solution being 3 or more mg/dl.

[Claim 12]A hemanalysis meter in which a reference solution group given in one claim of claim 1 to claims 3 is characterized by bilirubin concentration in a reference solution being

0.3 or more mg/dl.
[Claim 13]A hemanalysis meter in which a reference solution group given in one claim of claim 1 to claims 3 is characterized by a cholesterol concentration range in a reference solution being 133 or more mg/dl.
[Claim 14]A hemanalysis meter in which a reference solution group given in one claim of claim 1 to claims 3 is characterized by a triglyceride density range in a reference solution being 40 or more mg/dl.
[Claim 15]Measured value by said measuring formula which obtained said amendment data using a sample for amendment whose at least one or more measuring object component concentration is known, The hemanalysis meter according to claim 2 which is a difference of said measured value and known concentration which are produced from an error during a day of measurement, and an error between apparatus, and is characterized by said difference being subtracted and added by measured value about a blood sample.
[Claim 16]A means to enter light in a sample given in one claim of claim 1 to claims 3 is a sample cell, A hemanalysis meter being what has a mechanism which introduces a sample into the surface of attenuated-total-reflection prism, and is discharged, and spreads [which spreads and enters it] and emits light from said infrared light source to said attenuated-total-reflection prism.
[Claim 17]A hemanalysis meter, wherein a means to enter light in a sample given in one claim of claim 1 to claims 3 is a sample cell and is what introduces a sample into the surface of attenuated-total-reflection prism, and spreads [which spreads and enters it] and emits light from an infrared light source to said attenuated-total-reflection prism.
[Claim 18]A hemanalysis meter, wherein the attenuated-total-reflection prism according to claim 16 or 17 consists of zinc selenide, germanium, silicon, sapphire, etc.
[Claim 19]A hemanalysis meter, wherein a spectral means in a hemanalysis meter given in one claim of claim 1 to claims 3 is either of the Fourier spectra which used a concave grating, a spectral prism, or an interferometer.
[Claim 20]A hemanalysis meter, wherein a memory measure given in one claim of claim 1 to claims 3 is a storage of an IC memory [or] built in an arithmetic processing means, an optical disc attached to an arithmetic processing means, a magnetic disk, or a magneto-optical disc etc.

[Translation done.]